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The relationship between advanced maternal age and adverse pregnancy outcomes

İsa Temur

Department of Obstetrics and Gynecology, Faculty of Medicine, Niğde Ömer Halisdemir University, Niğde, Turkiye

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ABSTRACT

Aims: This study aimed to evaluate the impact of advanced maternal age on pregnancy and neonatal outcomes.

Methods: In this retrospective study, singleton pregnancies delivered at a tertiary care center between January 2021 and December 2023 were assessed. Participants were divided into two groups based on maternal age at delivery: 18–35 years and >35 years. Maternal and perinatal outcomes were compared between the groups using Chi-square tests.

Results: The mean maternal age was 32.12±5.37 years (range: 19–45 years). For women aged ≥35 years, the mean age was 38.27±2.66 years, while for those under 35 years, it was 25.98±4.28 years. No statistically significant differences were observed between the groups in terms of gestational diabetes mellitus, placental abruption, placenta previa, macrosomia, 5th-minute Apgar score, stillbirth, or the need for neonatal intensive care (p>0.05). However, pregnancy-induced hypertensive disorders, preterm birth, and postpartum hemorrhage (PPH) were significantly more common in women over 35 years (p=0.033, p=0.039, and p=0.043, respectively). Maternal age was identified as a significant positive predictor for preterm birth, PPH, and hypertensive disorders of pregnancy, with preterm birth being the most strongly associated. Receiver operating characteristic (ROC) analysis revealed optimal maternal age cutoff values for predicting adverse outcomes as follows: >37 years for preterm birth (AUC=0.687; p<0.001) and >33 years for pregnancy-induced hypertensive disorders (AUC=0.633; p=0.006).

Conclusion: The risk of pregnancy-induced hypertensive disorders, preterm birth, and PPH increases with maternal age. These findings underscore the need for enhanced antenatal monitoring in women of advanced maternal age.

Keywords: Advanced maternal age, preterm birth, postpartum hemorrhage, pregnancy-induced hypertensive disorders

INTRODUCTION

Advanced maternal age (AMA) is commonly defined as childbirth in women over the age of 35.[1] The global prevalence of AMA has been steadily increasing.[2] Several factors contribute to this trend, including shifts in social and economic conditions, higher levels of educational attainment, and advancements in reproductive healthcare that have improved access to fertility services.[3,4] Moreover, the widespread use of assisted reproductive technologies has enabled women to conceive well into their forties.[5]

Numerous studies have examined the association between maternal age and pregnancy outcomes, although findings remain inconsistent.[6] Some research has identified AMA as a significant risk factor for adverse perinatal outcomes such as gestational diabetes, preeclampsia, placenta previa, cesarean delivery, preterm birth, low birth weight, maternal mortality, and perinatal death.[3,7] Conversely, other studies have failed to demonstrate a strong association between AMA and these complications.[2,4,8]

The potential impact of maternal age on pregnancy outcomes remains a subject of ongoing debate. This study aims to clarify the hypothesis that AMA is associated with an increased risk of obstetric and neonatal complications.[9] Specifically, we sought to evaluate the influence of AMA on various pregnancy outcomes, including mode of delivery, preterm birth, pregnancy-induced hypertensive disorders, gestational diabetes mellitus (GDM), placenta previa, placental abruption, postpartum hemorrhage (PPH), macrosomia, 5th-minute Apgar score, stillbirth, and the need for neonatal intensive care.

METHODS

Ethics

This study was approved by the Non-interventional Ethics Committee of Niğde Ömer Halisdemir University Faculty of Medicine (Date: 19.09.2024, Decision No: 2024/83). The study was conducted in accordance with the principles of the latest version of the Declaration of Helsinki.

Corresponding Author: İsa Temur, t.isatemur@gmail.com

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Study Design and Participants
This retrospective study included women who delivered at the Obstetrics and Gynecology Clinic of Niğde Ömer Halisdemir University Hospital between January 2021 and December 2023. During the study period, approximately 9.000 deliveries were recorded. Based on maternal age at delivery, 200 women were categorized into two groups: those aged 18–35 years and those aged 35–45 years (100 participants per group).

Sample Size Determination
The effect size in this study was calculated as 0.477, which is considered a medium effect according to Cohen's classification (small=0.2, medium=0.5, large=0.8). Based on this effect size, a power analysis assuming 100 participants per group yielded a statistical power of 95%, indicating strong reliability. A power of 95% reflects a high probability of detecting a true effect, minimizing the risk of a type II error (β=0.05). This high power is a major strength in terms of the study's validity, as it reduces the likelihood of failing to detect real associations due to insufficient sample size.[10,11]

Study Variables
Perinatal outcomes were evaluated in relation to the following parameters: mode of delivery, preterm birth, pregnancy-induced hypertensive disorders, GDM, placenta previa, placental abruption, PPH, macrosomia, 5th-minute Apgar score, stillbirth, and the need for neonatal intensive care unit (NICU) admission.

Stillbirth was defined as fetal death at ≥22 weeks of gestation or with a birth weight of ≥500 grams in cases where gestational age was unknown. This definition also included intrapartum deaths. Preterm birth was defined as delivery occurring before 37 completed weeks of gestation, whether spontaneous or medically indicated. Hypertensive disorders were clinically diagnosed by gynecologists based on standard guidelines. This group included patients with chronic hypertension, gestational hypertension, preeclampsia, HELLP syndrome, or combinations thereof. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.

- Preeclampsia was defined as new-onset hypertension after 20 weeks of gestation accompanied by proteinuria (≥0.3 g protein in a 24-hour urine sample or ≥30 mg/dl on a random urine test).
- Gestational hypertension was defined similarly but without proteinuria.
- Eclampsia was defined as preeclampsia accompanied by seizures.
- Chronic hypertension was diagnosed when hypertension was present before 20 weeks of gestation.[12]

GDM was diagnosed based on results from a 75-g oral glucose tolerance test (OGTT) performed during pregnancy. Diagnostic thresholds included fasting glucose >90 mg/dl, ≥180 mg/dl at 1 hour, and ≥155 mg/dl at 2 hours.[13] Both insulin-dependent and non-insulin-dependent patients were included in the GDM group. The diagnosis of placenta previa (complete or marginal) was confirmed via ultrasound between 32 and 35 weeks of gestation. Both vaginal and cesarean deliveries (elective and emergency) were analyzed.

Exclusion Criteria
Multiple pregnancies and pregnancies with fetal anomalies were excluded from the study.

Data Collection
Data including demographic characteristics, medical and obstetric history, pregnancy progression, and perinatal outcomes were obtained from the hospital's electronic obstetric database.

Statistical Analysis
The data obtained from the study were evaluated with SPSS 22.0 package program. The compatibility of the variables with normal distribution was analyzed by Kolmogorov-Smirnov/Shapiro-Wilk tests and homogeneity of variances was analyzed by Levene's test. Descriptive statistical methods (number, percentage, mean and SD) were used for the individual characteristics of the participants. Receiver operating characteristic (ROC) curve analysis and hierarchical binomial logistic regression analysis were used. Pearson Chi-square test and regression analysis were used in the analyses and $p<0.05$ was considered significant.

RESULTS
The mean age of the pregnant women was 32.12±5.37 years (range: 19–45). For women aged 35 years and older, the mean age was 38.27±2.66 years (range: 35–45), while for women aged 35 years and younger, it was 25.98±4.28 years (range: 19–34). It was found that 36.5% of the pregnant women had a gravidity of four or more, and 28.5% had a parity of one. Additionally, 71% of the pregnant women gave birth between 38 and 42 weeks, including 65% of those aged 35 years and older and 77% of those younger than 35 years.

Among pregnant women under 35 years of age, 12% had GDM, 10% had pregnancy-induced hypertensive disorders, 8% had placental abruption and placenta previa, and 13% had macrosomia. In contrast, among pregnant women aged 35 years and older, 18% had GDM, 16% had pregnancy-induced hypertensive disorders, 11% had placental abruption, 9% had macrosomia, and 5% had placenta previa. When the occurrence of pregnancy-related risky conditions was evaluated according to age, it was found that only pregnancy-induced hypertensive disorders increased with age, and this difference was statistically significant (p=0.033) (**Table 1**).

While 57% of pregnant women under 35 years of age delivered vaginally, 23% experienced preterm birth, and 8% had PPH, 46% of pregnant women aged 35 years and older delivered vaginally, 35% experienced preterm delivery, and 17% had PPH. In the analysis of neonatal outcomes, the 5th minute APGAR score was 14%, stillbirth rate was 2%, and the need for neonatal intensive care was 15% among women under 35 years of age, compared to a 5th minute APGAR score of 19%, stillbirth rate of 2%, and neonatal intensive care need of 21% among women aged 35 years and older. When the postpartum period was evaluated according to the age variable, preterm

Table 1. Pregnancy outcomes of pregnant women according to age

Features	Pregnant women under 35 years of age, n (%)	Pregnant women aged 35 years and older, n (%)	Total, n (%)	p-value
Gestational diabetes mellitus	12 (12.0%)	18 (18.0%)	30 (15.5%)	p=0.322
Pregnancy-induced hypertensive disorders	10 (10.0%)	22 (22.0%)	32 (16.0%)	p=0.033
Abruption of placenta	8 (8.0%)	11 (11.0%)	19 (9.5%)	p=0.631
Macrosomia	13 (13.0%)	9 (9.0%)	22 (11.0%)	p=0.499
Placenta previa	8 (8.0%)	5 (5.0%)	13 (6.5%)	p=0.631
Preterm birth (<37 weeks)	23 (23.0%)	35 (35.0%)	58 (29.0%)	p=0.065

X^2=Pearson Chi-square test

birth and PPH were found to increase with age, and the differences were statistically significant (p=0.039, p=0.043) (**Table 2**).

Table 3 presents the results of the linear regression analysis conducted to evaluate the predictive effect of maternal age on specific obstetric complications. The findings indicate that AMA is a significant and positive predictor of preterm birth, PPH, and pregnancy-induced hypertensive disorders. Examination of the standardized beta (β) coefficients reveals that the relative impact of maternal age on these risk factors is ranked as follows: preterm birth, PPH, and pregnancy-induced hypertensive disorders. Moreover, the unstandardized regression coefficients (B) and their corresponding 95% confidence intervals support the statistical robustness of these associations (**Table 3**).

In **Table 4**, the ROC analysis identified maternal age >37 as the optimal cutoff value for predicting adverse pregnancy outcomes, specifically preterm birth. The area under the ROC curve (AUC) for this threshold was 0.687 (p<0.001) (**Figure 1**), indicating a higher likelihood of preterm birth in individuals older than 37 years. Similarly, for predicting pregnancy-induced hypertensive disorders, the optimal maternal age cutoff was >33 years, with an AUC of 0.633 (p=0.006) (**Figure 2**), suggesting an increased risk of hypertensive disorders in women older than 33 years.

Table 5 shows that there was no significant difference between preterm delivery and pregnancy-induced hypertension when comparing the frequency of composite adverse outcomes in women under and over 35 years of age (p=0.421).

DISCUSSION

The number of pregnancies among women of AMA has increased significantly worldwide, and this trend is expected to continue in the coming years. This demographic shift is associated with an elevated risk of complications affecting both maternal and neonatal health.

In our study, regression analysis revealed that AMA was significantly associated with an increased risk of pregnancy-related hypertensive disorders, preterm delivery, and PPH. AMA was identified as a positive and statistically significant predictor for each of these adverse outcomes. To quantify these risks, ROC analysis was performed to determine optimal

Table 2. Birth outcomes of pregnant women according to age

Features	Pregnant women under 35 years of age, n (%)	Pregnant women aged 35 years and older, n (%)	Total, n (%)	p-value
Type of birth-vaginal delivery Type of birth-caesarean section	57 (57.0%) 43 (43.0%)	46 (46.0%) 54 (54.0%)	103 (51.5%) 97 (48.5%)	X^2=2.422 p=0.078
Preterm birth	16 (16.0%)	29 (29.0%)	45 (22.5%)	X^2=3.676 **p=0.039**
5th-minute Apgar ≤ 7	14 (14.0%)	19 (19.0%)	33 (16.5%)	X^2=0.907 p=0.223
Stillbirth	2 (2.0%)	2 (2.0%)	4 (2.0%)	X^2=0.000 p=0.689
Neonatal intensive care need	15 (15.0%)	21 (21.0%)	36 (18.0%)	X^2=1.220 p=0.179
Postpartum hemorrhage	8 (8.0%)	17 (17.0%)	25 (12.5%)	X^2=3.703 **p=0.043**

X^2=Pearson Chi-square test

Table 3. Results of the linear regression analysis predicting obstetric characteristics by age variable

	Scales	B (95% CI)	t	β	R^2	F	p
Age variables	Preterm birth	7.914(2.21-13.62)	2.573	.180	.032	6.620	0.000
	Postpartum hemorrhage	8.274(0.60-15.94)	2.119	.149	.022	4.492	0.035
	Pregnancy-induced hypertensive disorders	8.296(1.35-15.25)	5.351	.166	.027	5.579	0.019

B: Unstandardized coefficient of regression, β: Standardized coefficient of regression, R^2: Coefficient of determination

Table 4. ROC analyses to determine maternal age cut-off point for predicting adverse pregnancy outcomes

Scales	AUC	p value	Cut-off point	Sensitivity	Descriptiveness	PLR	NLR
Preterm birth	0.687	<0.001	>37	53.33	78.06	2.43	0.60
Postpartum hemorrhage	0.623	0.069	>35	64.00	65.71	1.87	0.55
Pregnancy-induced hypertensive disorders	0.633	0.006	>33	78.12	52.98	1.66	0.41

ROC: Receiver operating characteristic, AUC: Area under the ROC curve, PLR: Positive likelihood ratio, NLR: Negative likelihood ratio

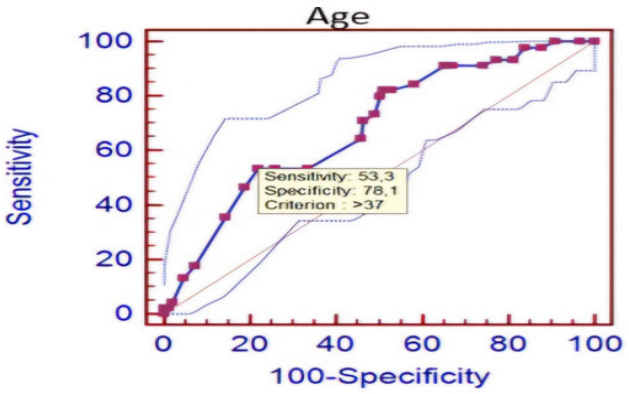

Figure 1. Cut-off point value for maternal age predicting preterm birth >37 (AUC= 0.687, p<0.001)

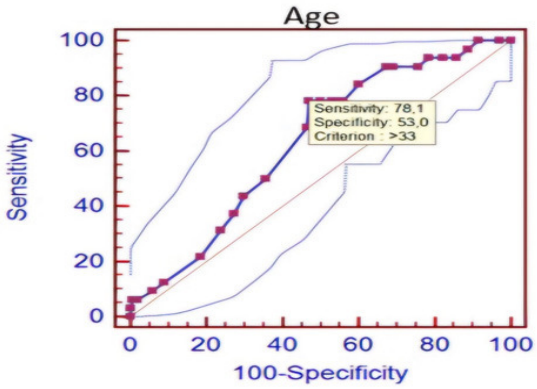

Figure 2. Cut-off point value of and pregnancy-induced hypertensive disorders predicting maternal age >33 (AUC= 0.633, p=0.006)

maternal age cut-off values. The analysis identified >33 years as the optimal threshold for predicting pregnancy-induced hypertensive disorders (AUC=0.633, p=0.006), and >37 years for predicting preterm birth (AUC=0.687, p<0.001).

In clinical research, a composite outcome refers to the combination of multiple clinically relevant endpoints into a single metric, allowing for a more holistic assessment of overall health status or treatment efficacy. In our study, no statistically significant difference was observed in the frequency of composite adverse outcomes—specifically preterm birth and pregnancy-induced hypertension—between women under and over 35 years of age. This non-significant result may be attributed to the limited number of participants experiencing these complications, thereby reducing the statistical power to detect group differences.

An increased incidence of gestational hypertensive disorders among women of AMA has been frequently reported in the literature.[7,28,33] In particular, the heightened risk of early-onset preeclampsia is often attributed to age-related vascular endothelial damage and dysfunction, which can compromise the maternal cardiovascular system's ability to adapt adequately to pregnancy.[14] Similarly, Timofeev et al.[15] reported that the risk of pregnancy-induced hypertension increases with advancing age in women over 35 years. In contrast, Cleary-Goldman et al.[16] found that women aged 35–39 had a lower risk of pregnancy-induced hypertension compared to those under 35. Likewise, a study conducted in Turkiye by Çakmak Çelik et al.[17] reported no significant difference in the incidence of preeclampsia among women in the AMA group.

These contradictory findings suggest that although advancing maternal age may contribute to vascular pathologies that predispose women to preeclampsia, other individual and environmental factors likely play a decisive role in this association. Our study's findings underscore the importance of regular blood pressure monitoring in women over the age of 35. These results can inform both preconception and antenatal counseling strategies. Moreover, encouraging home-based blood pressure monitoring during the third trimester may offer an effective approach for early detection and intervention in this high-risk population.

The literature presents conflicting findings regarding the risk of PPH. While earlier studies have linked advanced AMA to an increased risk of PPH, a definitive consensus has yet to be reached.[18,19] For example, Kramer et al.[19] reported that maternal age of 35 years is associated with a heightened risk of postpartum bleeding. Similarly, Sheen et al.[18] suggested that women over the age of 45 face the highest risk of PPH during delivery-related hospitalizations. In contrast, a meta-analysis found no significant association between maternal age of 35 and the risk of PPH.[20] Furthermore, Lao et al.[21] reported that advancing maternal age may actually be associated with a reduced risk of PPH, with incidence rates declining progressively from the 25–29 age group to those aged ≥40.

Table 5. Comparison of the frequency of composite adverse outcomes in women under and over 35 years of age

Features	Pregnant women under 35 years of age (n=100)		Pregnant women aged 35 years and older (n=100)		Total (n=200)		Test
	n%		n%		n%		
Preterm birth+pregnancy-induced hypertensive disordes							
Yes	6	6.0	9	9.0	15	7.5	X^2=0.649
No	94	94.0	91	91.0	185	92.5	p=0.421

X^2=Pearson Chi-square test

In our study, we observed an increased risk of PPH among women of AMA. Several physiological mechanisms may contribute to this finding. One possible explanation is the age-related decline in oxytocin receptor density and desensitization due to prolonged oxytocin exposure, both of which may impair uterine contractility.[22] This condition can result in uterine atony and subsequently elevate the risk of PPH. Additional contributing factors may include uterine muscle fatigue following prolonged labor and impaired contractility associated with cesarean delivery. Collectively, these mechanisms render older mothers more susceptible to PPH. Therefore, in cases where additional risk factors for PPH are present, healthcare providers should consider early preparation of blood products as part of the delivery plan to ensure timely intervention and improve maternal outcomes.

Although the precise etiology of preterm birth remains unclear, one of the most widely accepted underlying mechanisms involves placental vascular pathology. Spontaneous preterm birth has been associated with placental hemorrhage, compromised vascular integrity, and inadequate remodeling of the maternal spiral arteries.[23] Additionally, preeclampsia and other hypertensive disorders may contribute to preterm birth through uteroplacental ischemia.

In the context of AMA, declining progesterone levels may represent an additional contributing factor. Low progesterone concentrations have been linked to an increased risk of preterm birth, whereas progesterone supplementation has demonstrated preventive efficacy.[24] Numerous studies have reported that women of AMA are at greater risk of preterm delivery and giving birth to low birth weight infants compared to younger counterparts.[25,26] Similarly, other research has also identified elevated rates of preterm birth among older mothers.[7] Our findings are consistent with these studies. However, a study conducted by Schimmel et al.[5] found no statistically significant association between AMA and preterm birth. Such conflicting results may be attributable to variations in sociodemographic profiles and clinical risk factors across different populations. Nevertheless, the most plausible explanation for the increased incidence of preterm birth in AMA is the higher prevalence of pregnancy-related complications in this group.

In our study, AMA was not significantly associated with differences in mode of delivery, the incidence of gestational diabetes, placental abruption, placenta previa, macrosomia, 5-minute Apgar scores, stillbirth, or the need for neonatal intensive care.

AMA has been associated with adverse lipid profiles, including decreased insulin sensitivity and elevated levels of triglycerides and cholesterol, all of which may contribute to impaired glucose tolerance and an increased risk of gestational GDM.[7,26] Clinical studies have shown that insulin resistance tends to increase with age, often resulting in mild hyperglycemia. In a study conducted by Yogev et al.[7] in Israel, the prevalence of GDM rose markedly with advancing age: 1.4% among women aged 20–29, 4.2% in those aged 30–39, 10.2% in the 40–44 age group, and 17% in women aged 45 and older. Furthermore, Cleary-Goldman et al.[16] identified maternal age ≥40 as an independent risk factor for the development of GDM.

In our study, a rising trend in the prevalence of GDM was observed with increasing maternal age; however, this difference did not reach statistical significance. This outcome contrasts with a recent study by Iman et al.[27], who divided maternal age into three categories and reported a significantly higher risk of GDM among women aged 31–40 years. In our study, maternal age was classified into only two groups, and the relatively small sample size in the AMA group may have limited the statistical power to detect significant differences. Future research employing more refined age stratifications and ensuring adequate representation within each subgroup may yield a more accurate evaluation of the relationship between maternal age and GDM risk. Nevertheless, considering the well-documented physiological effects of aging on glucose metabolism, this observation may still hold clinical relevance. GDM has been linked to various adverse outcomes, including increased rates of cesarean delivery, macrosomia, low Apgar scores, preterm birth, and admissions to the NICU.[7] Therefore, our findings may serve as a useful clinical indicator of the potential risks associated with GDM in women of AMA.

In our study, analysis of delivery mode data revealed that 54% of pregnant women aged over 35 years underwent cesarean section (CS), compared to 43% of women under 35 years of age. Karlström et al.[28] reported that CS rates were two to four times higher among older pregnant women compared to younger reference groups. Similarly, Pawde et al.[29] observed elevated CS rates in women over 35, although the difference was not statistically significant. Ritzinger[32] and Usta et al.[30] attributed the rising CS rates not only to medical indications but also to heightened physician and maternal anxiety related to AMA, previous obstetric complications, and negative birth experiences among multiparous women. In addition, clinical indications play a major role in the increased CS rates. Goldmann et al.[16] emphasized that preterm labor and obstetric complications were more prevalent among older women, leading to a greater reliance on cesarean deliveries. In line with these findings, our study also demonstrated that maternal complications associated with advanced age likely contributed to the higher CS rates observed in this group.

In our study, no significant association was found between AMA and either placental abruption or placenta previa, likely due to the low incidence of these conditions. However, existing literature suggests that AMA may increase the risk of both conditions, particularly in the presence of additional risk factors such as multiparity and hypertension.[7,18] Population-based studies have demonstrated a significant association between AMA and a higher likelihood of placenta previa. For example, Biro et al.[31] identified AMA as an independent risk factor for placenta previa. Similarly, Cleary-Goldman et al.[16] attributed this increased risk to progressive vascular damage associated with aging. Conversely, some researchers argue that when varying risk profiles are taken into consideration, maternal age alone may not be a decisive factor in the development of placenta previa.[32]

Nevertheless, the elevated risk of placenta previa in older women has important implications not only for individual

clinical outcomes but also from a broader public health perspective. The growing number of pregnancies among women of advanced age may lead to increased rates of hospitalizations, cesarean deliveries, and blood transfusion needs associated with placenta previa. Therefore, meticulous monitoring and strategic clinical planning are essential in the management of this high-risk population.[7]

In this study, the impact of AMA on neonatal outcomes was also assessed. Our analysis revealed no statistically significant differences between the age groups in terms of stillbirth, NICU admission, 5-minute Apgar scores, or macrosomia. However, the literature presents mixed findings on this topic. Some studies have reported no differences in Apgar scores among infants born to older mothers,[6,30] while others have found lower Apgar scores and higher NICU admission rates in this population.[7,33] Conversely, several studies have reported no significant differences in either Apgar scores or NICU length of stay.[25] These inconsistencies may be explained by variations in sociodemographic characteristics and clinical risk profiles among study populations.

Despite a higher frequency of antenatal complications among women aged 35 and above in our study, neonatal outcomes were comparable to those observed in younger mothers. This finding suggests that early diagnosis, appropriate follow-up, and timely interventions can effectively improve neonatal outcomes in high-risk pregnancies. Moreover, protective strategies—such as the administration of antenatal corticosteroids, a conservative approach to cesarean delivery, and childbirth occurring in perinatal care centers—may have contributed to these favorable outcomes. Collectively, these results imply that older mothers can potentially mitigate the risks associated with pregnancy complications by engaging more consistently in prenatal care.

Limitations

One of the strengths of our study is the high quality of the registry and its consistency with birth records. We conducted a comprehensive analysis of pregnancy, delivery, and neonatal outcomes associated with AMA. The sample size was sufficient to capture the obstetric challenges linked to AMA pregnancies during the study period. However, the retrospective design represents a limitation, and the study did not include data from a national cohort. Furthermore, some important sociodemographic variables—such as body-mass index (BMI) and socioeconomic status—were not available. As a result, we were unable to assess the impact of prenatal screening tests or fetal chromosomal abnormalities. Since the study population included only women aged 35 years and older, the statistical power to detect rare outcomes was limited. Subgroup analyses evaluating the effects of very AMA could not be performed. In AMA pregnancies, it is essential to inform patients about potential maternal and neonatal complications and to establish follow-up protocols tailored to this group. Given the inconsistencies in the literature, further studies are needed to address these gaps.

CONCLUSION

Our results emphasize the importance of informing women over 35 years of age about PPH, preterm delivery risks, and the need for blood pressure control.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the University Medical Faculty Clinical Researches Ethics Committee (Date:19.09.2024, Decision No: 2024/83).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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